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EXAMINER
CARLSON, KAREN C

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 09/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/709,585	VINIK ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-8,11,12,14-18 and 21-36* is/are rejected.

7)☒ Claim(s) *2,4,9,10,13,19 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2- IDSs* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Priority date is February 22, 1995.

The second preliminary amendment filed October 3, 2001, said amendment adding Claims 29-36, has not been entered because the new claims have not been underlined in accordance to Rule 1.173. However, this Office Action takes into consideration these claims 29-36 as though they were entered in order to advance prosecution. Applicants are entrusted with properly adding these new claims in response to this Office Action, OR accepting the addition of these claims as an Examiner's Amendment as proposed at the end of this Office Action.

Reissue (not entered as per above) Claims 29, 30, 33, and 34 are barred by recapture because Applicants are precluded from recapturing subject matter surrendered in order to obtain the original patent. Original Claim 3, for example, drawn to a polypeptide comprising at least 15 consecutive amino acids of an INGAP protein was rejected under 35 USC 112, first paragraph, for scope in the first action on the merits (Paper #11 mailed December 10, 1996), said rejection maintained in the rejection mailed July 23, 1997 (Paper #14). Claim 3 was amended to recite a function in Amendment D, Paper #15, filed October 23, 1997, and allowance was granted January 20, 1998 (Paper #16). Claims 29, 30, 33, and 34, while reciting a polypeptide comprising at least 15 amino acids from SEQ ID NO: 2, still recite a fragment without a function in a similar fashion to original Claim 3. Therefore, these claims are barred by recapture.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 8, 15, 17, 18, 25, and 26, and 29-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claims 7 and 17, it is not clear what biological activity is being referred to. Further, claims 7 and 17 depend from Claims 3 and 14, respectively, wherein a biological activity is already recited. Therefore, it is not clear why these claims (and 8 and 18) refer to biological activity in a generic sense, thus broadening the scope of the independent claims.

Claim 11, "eogenesis" should be written "neogenesis".

In Claim 15, it is not clear if it is the "at least 15 amino acids" of INGAP or the second polypeptide that provides the beta cell stimulatory activity.

Claims 25 and 26 states that the vector encodes INGAP. It is more accurate to state that the vector comprises a nucleic acid encoding INGAP, for example.

Claims 29 –36 use the acronym INGAP without providing its definition. Additionally, these new claims appear awkward, that is, are the 15 amino acids a length of any amino acid found in SEQ ID NO: 2, or a fragment of SEQ ID NO: 2?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5-8, 11, 12, 14-18, 21-29, and 33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to protein which is not defined by structure and function. For example, many proteins have islet neogenesis function and ilotropin is cited below for example. Without structure correlated with function, one cannot know which proteins are in Applicants possession. Therefore, the specification lacks written description of the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 7, 8, 12, 14, 17, 18, 21, 25, 26, 27, and 28 are rejected under 35 U.S.C. 102(a) as being anticpated by Watanabe et al. (April, 1994; PNAS 91:3589-3592). Watanabe et al. teach a preparation of recombinantly produced (see abstract, introduction, results) Reg protein from rat (page 3590; Fig 1) having the ability to stimulate the regeneration and growth of pancreatic beta cells (page 3591). Thus, Watanabe et al. teach a mammalian islet neogenesis associated protein (Claim 1) that is expressed from a host cell via a vector comprising nucleic acid encoding Reg (Claim 25, 26) that is free of other proteins (Claim 21, 27, 28). The rat Reg protein is 165 amino acids in length (see introduction) and is therefore at least 15 amino acids long (Claim 3, 7, 8). Watanabe et al. teach that Reg protein was administered to rats and therefore Reg protein was placed in a pharmaceutical composition (Claims 12, 14, 17, 18).

Claims 1, 3, 6, 7, 8, 11, 12, 14, 17, 18, 21, 22, 25, 26, 27, and 28 are rejected under 35 U.S.C. 102(b) as being anticpated by Pettenger et al. 1992. Pettenger et al. teach ilotropin, a pancreatic protein obtained from hamster (mammalian) that stimulates the growth or neogenesis of pancreatic islet cells. Thus, ilotropin is a naturally occurring mammalian islet neogenesis associated protein (Claim 1). Ilotropin has a molecular weight of 29-44 kD on SDS-PAGE and is therefore free of other proteins (Claim 21, 22). Because ilotropin is a protein of 29-44 kD, and therefore has an Examiner-estimated amino acid length of 290-440 amino acids,

ilotropin is at least 15 amino acids in length (Claim 3, 7, 8). Ilotropin was increased in cytosolic extracts of cellophane wrapped pancreas (page 126, para. 1; Claim 11). Cytosolic extracts comprising ilotropin were injected into 7-8 week old female Syrian hamsters (page 124); therefore, pharmaceutical compositions of ilotropin and a pharmaceutical carrier (Claim 12, 14, 17, 18) that is substantially free of other proteins (Claim 27, 28) is taught by Pettenger et al. The purified cytosolic extracts comprising ilotropin was applied to Separose12 FPLC columns and eluted at pH 7. Bioactivity was detected in fractions 3 and 4, corresponding to ilotropin molecular weight (Fig 2 and pages 126-127). Therefore, ilotropin is able to conjugate to a solid support (Claim 6).

Claims 25 and 26 are also considered to be anticipated by Pettenger et al. because there appears to be no distinguishing feature to ilotropin by expressing it from a host cell.

It is noted that Pettenger et al. (and a similar teaching of Rosenburg) were overcome in the previous prosecution (of SN 08/401,530) because Applicants urged (in Paper #12 filed April 10, 1997 at page 7) that the molecular weight of INGAP is about 18 kD (174 amino acids), or about half that taught for ilotropin and therefore ilotropin and INGAP are distinguished from each other. While this observation may be a distinguishing factor, the claims do not recite any limitation that distinguishes INGAP from ilotropin. Therefore, this reference against the claims is being re-iterated.

Note also that the molecular weight of INGAP SEQ ID NO: 2 is not set forth in the specification. Amending the claims to include this molecular weight to distinguish over Pettenger et al. would be considered to be new matter.

Claims 2, 4, 9, 10, 13, 19, and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Art of Record

The Reg protein deduced amino acid sequence has been presented in the art –see Terazono et al. (1988; J. Biol. Chem. 263(5(: 2111-2114) and Rouquier et al. (1991; J. Biol. Chem. 266(2): 786-791) and references 4-11 cited in Watanabe et al. However, none of these references teach a "preparation" of the Reg protein. With all of these teachings of the Reg protein, it would appear that it would have been obvious for anyone of these references to have expressed and isolated the Reg protein, that is, to make a preparation of the Reg protein before Watanabe et al. in April 1994. Further, without the Reg protein in hand, its activity is conjecture. Because this art of record cited here does not teach or suggest to isolate the Reg protein, it appears that skilled artisans did not find motivation to isolate Reg, or that it was difficult and therefore unpredictable to purify and isolate Reg. Therefore, these art of record will be simply noted by the Examiner to render the record of prior art complete.

The following claim amendments are suggested to overcome the rejections set forth above. If Applicants wish, these claims can be entered by examiner's amendment.

1. A purified preparation of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein) [substantially free of other mammalian proteins], wherein said INGAP protein comprises amino acid sequence SEQ ID NO: 2.

Cancel Claim 2 because it is redundant if Claim 1 is amended as shown above.

3. A purified preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), wherein said INGAP protein comprises amino acid sequence SEQ ID NO: 2, wherein said polypeptide has immunogenic activity [and wherein said polypeptide is a portion of INGAP protein].

4. A polypeptide which is a fusion of (1) as sequence of at least 15 consecutive amino acids of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), wherein said INGAP protein comprises amino acid sequence SEQ ID NO: 2, wherein said polypeptide has immunogenic activity [to] and (2) a second polypeptide derived from a second protein.

5, 6, -- OK
Cancel Claim 7.

8. [The preparation of claim 7 wherein said biological activity is] A purified preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), wherein said INGAP protein comprises amino acid sequence SEQ ID NO: 2, wherein said polypeptide has the ability to stimulate pancreatic duct cells to grow and proliferate.

9, 10 –OK

11. A preparation of an islet neogenesis associated protein (INGAP protein) of a mammal substantially purified from other proteins of the mammal wherein said INGAP protein is inducible upon cellophane-wrapping of the pancreas of the mammal, wherein said INGAP protein comprises SEQ ID NO: 2.

It seems that claim 11 doesn't provide more than claim 1 – cancel? Note that the cellophane wrapping does not distinguish this claimed protein from ilotropin.

12. A pharmaceutical composition for the treatment of pancreatic insufficiency, comprising:

a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), wherein said INGAP protein comprises amino acid sequence SEQ ID NO: 2, and

a pharmaceutically acceptable diluent or carrier.

Cancel claim 13 –redundant if claim 12 is amended.
Cancel Claim 27 – does not appear to add a limitation to claim 12.

14. A pharmaceutical composition comprising:

a preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), wherein said INGAP protein comprises amino acid sequence SEQ ID NO: 2, wherein said polypeptide is capable of stimulating β cell regeneration of pancreatic ductal cells, and

a pharmaceutically acceptable diluent or carrier[, wherein said polypeptide is capable of stimulating β cell regeneration of pancreatic ductal cells, and wherein said polypeptide is a portion of said INGAP protein].

15. A pharmaceutical composition comprising:

a preparation of a polypeptide which a fusion of (1) a sequence of at least 15 consecutive amino acids of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), werein said INGAP protein comprises amino acid sequence SEQ ID NO: 2, wherein said polypeptide is capable of stimulating β cell regeneration of pancreatic ductal cells, [to] and (2) a second polypeptide derived from a second protein,

and a pharmaceutically acceptable diluent or carrier[, wherein said polypeptide is capable of stimulating β cell regeneration of pancreatic ductal cells].

16 –OK

Claims 17 and 18- cancel.

19, 20 –OK

Claims 21 and 22, 25 and 26, 27, 28 – cancel, does not appear to add a limitation to claim 1, 3, 11, 12 or 14.

Add the following new Claims:

29. A purified preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of the amino acid sequence shown in SEQ ID NO: 2, wherein said polypeptide is capable of stimulating β cell regeneration in pancreatic ductal cells.

30. The preparation of claim 29 wherein the polypeptide comprises a sequence of at least 15 consecutive amino acids selected from amino acids #103 to #122 as shown in SEQ ID NO: 2.

31. A pharmaceutical composition comprising a preparation of a polypeptide which comprises a sequence of at least 15 consecutive amino acids of the amino acid sequence shown in SEQ ID NO: 2, wherein said polypeptide is capable of stimulating β cell regeneration in pancreatic ductal cells.

32. The pharmaceutical composition of claim 31 wherein the polypeptide comprises a sequence of at least 15 consecutive amino acids selected from amino acids #103 to #122 of SEQ ID NO: 2.

33. A purified preparation of a polypeptide which consists of a portion of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), wherein said INGAP protein comprises amino acid sequence SEQ ID NO: 2, said polypeptide consisting of at least 15 consecutive amino acids of the amino acid sequence shown in SEQ ID NO: 2, wherein said polypeptide is capable of stimulating β cell regeneration in pancreatic ductal cells.

34. A preparation of claim 33 wherein the polypeptide consists of a portion of INGAP of at least 15 consecutive amino acids selected from amino acids #103 to #122 as shown in SEQ ID NO: 2.

35. A pharmaceutical composition comprising a polypeptide which consists of a portion of a naturally occurring mammalian islet neogenesis associated protein (INGAP protein), wherein said INGAP protein comprises amino acid sequence SEQ ID NO: 2, said polypeptide consisting of at least 15 consecutive amino acids of the amino acid sequence shown in SEQ ID NO: 2, wherein said polypeptide is capable of stimulating β cell regeneration in pancreatic ductal cells.

36. The pharmaceutical composition of claim 35 wherein the polypeptide consists of a portion of INGAP of at least 15 consecutive amino acids selected from amino acids #103 to #122 of SEQ ID NO: 2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 703-308-0034. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low can be reached on 703-308-2329. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

September 8, 2003

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER